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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/466,035	12/17/1999	MATTI SALLBERG	930049.458C1	9697

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NOVARTIS VACCINES AND DIAGNOSTICS INC.
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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
09/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/466,035	SALLBERG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,12,13 and 26-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12,13 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/12/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 5/12/08 has been entered. Claims 6-11, 14-25, and 30 are canceled. Claims 1-5, 12-13, and 26-29 are pending in the instant application. An action on the merits follows.

It is noted that those sections of Title 35, US code not included in this action can be found in the previous office action.

Information Disclosure Statement

Applicant's IDS filed on 5/12/08 has been considered by the examiner. An initialed copy is attached to this office action.

Claim Rejections - 35 USC § 112

The rejection of claims 1-5, 12-13, and 26-29 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of applicant's amendments to the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-5, 12-13, and 26-39 under 35 U.S.C. 103(a) as being unpatentable over WO 95/07994 (1995), hereafter referred to as Dubensky et al., in view of Hu

et al. (1991) AIDS Res. Hum. Retrovir., Vol. 7 (7), 615-620 is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant rejection for reasons of record as discussed in detail below.

The applicant reiterates their previous argument that since Hu et al. teaches the use of a prime boost strategy with a replicating vaccinia virus vector, the skilled artisan would not be motivated to combine the teachings of Hu et al. with those of Dubensky et al. who teaches the use of non-replicating vectors, i.e. alphavirus vectors or layered eukaryotic systems. More specifically, the applicant argues that the two different strategies of repeat vaccination with the same vector, versus vaccination with a vector and a protein, result in different kinds of immune responses, that Hu teaches away from using repeated virus immunizations, citing page 618, paragraph 3 of Hu et al., and that since post-filing publications by Greer et al. and White et al. show that repeat vaccinations with replication incompetent alphavirus vectors enhanced the immune response, the skilled artisan would not have been motivated to vaccinate with a replication incompetent virus and a protein. The applicant then states that Hu's response only makes sense for vaccinia virus where neither replication competent nor replication incompetent vector can be used repeatedly due to anti-vector responses, citing another post-filing publication by Sharpe et al. From the preceding arguments, the applicant concludes that there would have been no motivation to switch from the repeat administration of alphavirus taught by Dubensky et al. to a prime boost strategy with vector and protein.

In response, it is first noted that applicant's reliance on post-filing evidence, published in 2007 (Greer et al. and White et al.) and 2001 (Sharpe et al.) is not probative as to the obviousness of the invention at the time of filing. Knowledge added to the art years after the

effective filing date does not provide any evidence of what was known or predictable at the time of filing, which in this case is 1996. None of Greer et al., White et al., or Sharpe et al. make any statements as to the level of skill in the art of vaccination using replication competent or incompetent vectors prior to September, 1996. As such, applicant's reliance on such publications as evidence that the skilled artisan would not have been motivated to combine the teachings of Dubensky et al. and Hu et al. because post-filing experiments show that repeat administration with alphavirus enhances immune responses is not persuasive in establishing nonobviousness.

Regarding applicant's arguments that repeat vaccination with the same vector versus prime boost with a vector and protein results in "different types" of immune responses, this argument is not persuasive in showing that the skilled artisan would not have been motivated to modify the Dubensky methods by utilizing a combination of vector and protein since the Hu et al. reference clearly demonstrates in Table I that a prime/boost strategy using the same vector and a prime/boost strategy using a vector followed by a protein both result in the generation of antigen specific antibodies. Thus, clearly the use of vectors to induce an immune response and the use of a protein to induce an immune response are analogous in that they both induce antibody responses. Further, as discussed in detail in previous office actions, the same Table in Hu et al. provides motivation to use a prime/boost strategy where a vector immunization is followed by a protein immunization by demonstrating that this combination results in neutralizing titers of antibody.

Finally, the applicant argues that Hu teaches away from using a non-replicating vector by teaching the advantages of a replicating viral vector in the prime-boost regimen, pointing to

the abstract and Tables 1 and 2 of Hu et al. In response, it is not agreed that Hu's use of a "replicating" vaccinia virus teaches away from the use of a "non-replicating" vector, or that the skilled artisan would not have been motivated to use the prime-boost strategy of Hu with the replication incompetent vectors taught by Dubensky et al.. It is first noted that Dubensky et al. teaches the use of live recombinant alphavirus to stimulate immune responses which are either replication competent or replication incompetent. See for example pages 6 and 15 which discuss alphavirus vectors with modified viral junction regions. Further, Dubensky et al. teaches that the layered eukaryotic vector initiation systems comprises as a second layer a replicating construct which includes poxvirus, of which vaccinia virus is a subspecies, see pages 8 and 38. Thus, Dubensky et al. provides teachings that the replication status of the immunizing alphavirus or layered eukaryotic vector initiation system does not affect the ability of these expression systems to express a heterologous antigen and induce an antigen specific immune response. In addition, it is noted that Dubensky in pages 148-151 teaches non-replicating sindbis vectors encoding HBV or HIV antigens and the use of multiple administration of the vector to induce immune responses, i.e. prime and boost using the same vector. Thus, Dubensky et al. already provides motivation for following a prime and boost protocol to induce an antigen specific immune response using either replication competent or incompetent vectors. Dubensky et al. only differs from the instant invention as claimed by not teaching that protein antigen can be administered instead of the vector following the first vector administration.

Hu et al. was cited for teaching the benefits of "boosting" a live recombinant virus immunization with the immunizing protein itself instead of with a second immunization with

the recombinant virus. Further, it is disagreed that either the abstract or Tables 1 or 2 somehow "teach away" from the use of a "non-replicating" versus a "replicating" virus. In Table I, it is clear that immunization with a single dose of vaccinia virus encoding gp160, the "replicating" virus, does not induce greater amounts of antibody than administration of gp160 protein, compare week 8 ELISA titers from Group I and Group IV. Further, Table 1 provides motivation to boost with a protein rather than a second vector administration since Group 1, which received two administrations of the viral vector generated less antigen specific antibody at week 10 than Group II which received the virus and then the gp160 protein itself. Furthermore, as applicant themselves have noted in their responses to previous office actions, the art-recognized adverse effects of generating viral specific immune responses in addition to antigen specific immune responses using replicating virus would further motivate the skilled artisan to utilize a non-replicating rather than a replicating virus to generate antigen specific immune responses in an animal.

Therefore, it is maintained that since Dubensky et al. teaches that both replicating and non-replicating alphaviruses and layered eukaryotic vector initiation systems can induce antigen specific immune responses and further teaches a "prime and boost" protocol using multiple vector administrations, and since Hu et al. teaches that boosting with protein is more effective than boosting with vector, it would have been *prima facie* obvious to the skilled artisan at the time of filing to utilize the prime boost approach taught by Hu et al. in the immunization methods of Dubensky et al. Further, based on the state of the art in generating immune responses using replicating and non-replicating viruses, the skilled artisan would have had a reasonable expectation of success in generating an immune response by administering a

replication incompetent vector construct encoding a viral antigen followed or preceded by administration of the viral antigen itself.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology

center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633